FOOD AND DRUG ADMINISTRATION

CENTER FOR TOBACCO PRODUCTS

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

(TPSAC)

FRIDAY, MARCH 18, 2011

8:00 a.m. to 9:30 a.m.

FDA White Oak Campus

White Oak Conference Center

Building 31, The Great Room

Silver Spring, Maryland

This transcript has not been edited or corrected, but appears as received from the commercial transcribing service.

TPSAC Members (voting)

Jonathan M. Samet, M.D., M.S. *(Chair)*
Professor and Flora L. Thornton Chair,
Department of Preventive Medicine
Keck School of Medicine
University of Southern California, Los Angeles
Norris Comprehensive Cancer Center
1441 Eastlake Avenue, Room 4436, MS 44
Los Angeles, California 90089

Neal L. Benowitz, M.D.
Professor
Chief, Division of Clinical Pharmacology
Departments of Medicine and Biopharmaceutical Sciences
Schools of Medicine and Pharmacy
University of California, San Francisco, Box 1220
San Francisco, California 94143–1220

Mark Stuart Clanton, M.D., M.P.H.
Chief Medical Officer
American Cancer Society, High Plains Division
2433-A Ridgepoint Drive
Austin, Texas 78754

Karen L. DeLeeuw, M.S.W.
(Employee of a state or local government or of the Federal Government)
Director, Center for Healthy Living and Chronic Disease Prevention
Colorado Department of Public Health and Environment
4300 Cherry Creek Drive South
Denver, Colorado 80246

Dorothy K. Hatsukami, Ph.D.
Forster Family Professor in Cancer Prevention and
Professor of Psychiatry
Tobacco Use Research Center
University of Minnesota
717 Delaware St. SE
Minneapolis, Minnesota 55414

Patricia Nez Henderson, M.P.H., M.D.
(*Representative of the General Public*)
Vice President
Black Hills Center for American Indian Health
701 St. Joseph Street, Suite 204
Rapid City, South Dakota 57701

Jack E. Henningfield, Ph.D.
Vice President, Research and Health Policy
Pinney Associates
3 Bethesda Metro Center, Suite 1400
Bethesda, Maryland 20814

Melanie Wakefield, Ph.D.
Director, Centre for Behavioural Research in Cancer
The Cancer Council Victoria
1 Rathdowne Street
Carlton
Victoria, Australia 3053

TPSAC Members *(non-voting Industry Representatives)*

Luby Arnold Hamm, Jr.
(Representative of the interests of tobacco growers)
4901 Shallowbrook Trail
Raleigh, North Carolina 27616-6107

Jonathan Daniel Heck, Ph.D., DABT
(Representative of the tobacco manufacturing industry)
Lorillard Tobacco Company
A.W. Spears Research Center
420 N. English St., P.O. Box 21688
Greensboro, North Carolina 27420-1688

John H. Lauterbach, Ph.D., DABT

(Representative for the interest of small business tobacco manufacturing industry)

Lauterbach & Associates, LLC

211 Old Club Court

Macon, Georgia 31210-4708

***Ex Officio* Members** (non-voting)

Timothy McAfee, M.D., M.P.H.

Director, Office of Smoking and Health

National Center for Chronic Disease Prevention and Health Promotion

Centers for Disease Control and Prevention

4770 Buford Highway, N.E.

Koger Center, Columbia Building MS K-50

Atlanta, Georgia 30341

FDA Participants (non-voting)

Lawrence Deyton, M.S.P.H., M.D.

Director

Center for Tobacco Products

Food and Drug Administration

9200 Corporate Boulevard

Rockville, Maryland 20850-3229

Corinne G. Husten, M.D., M.P.H.

Senior Medical Advisor, Office of the Director

CTP/FDA

David L. Ashley, Ph.D.

Director, Office of Science, CTP/FDA

C O N T E N T S

P R O C E E D I N G S

(8:08 a.m.)

Call to Order

DR. SAMET: Good morning. We'll get started. I'm Jon Samet, the chair of the Tobacco Products Scientific Advisory Committee. I want to make a few statements, and then we'll introduce the committee.

For topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meeting will be a fair and open forum for discussion of these issues and that individuals can express their views without interruption. Thus as a gentle reminder, individuals will be allowed to speak into the record only if recognized by the chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take care that their conversations about the topics

at hand take place in the open forum of the meeting. We are aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topics during breaks. Thank you.

Caryn.

Conflict of Interest Statement

MS. COHEN: The Food and Drug Administration is convening today's meeting of the Tobacco Products Scientific Advisory Committee under the authority of the Federal Advisory Committee Act of 1972. With the exception of the industry representatives, all members and non-voting members are special government employees or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with federal ethics and conflict of interest laws, covered by but not

limited to those found at 18 U.S.C. Section 208 and Section 712 of the Federal Food, Drug and Cosmetic Act, is being provided to participants in today's meeting and to the public.

The FDA has determined that members of this committee are in compliance with federal ethics and conflict of interest laws. Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Under 712 of FD&C Act, Congress has authorized FDA to grant waivers to special government employees and regular federal employees with potential financial conflicts when necessary to afford the committee essential expertise. Related to the discussion of today's meeting, members of today's meeting have been screened for potential financial conflicts of interest of their

own as well as those imputed to them, including those of their spouses or minor children and, for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties and primary employment.

Today's agenda involves receiving an update on the Menthol Report Subcommittee and discussing presentations regarding the data requested by the committee at the March 30th and 31st, 2010 meeting of the Tobacco Products Scientific Advisory Committee. This is a particular matters meeting during which general issues will be discussed. Based on the agenda for today's meeting and all financial interests reported by the committee members, no conflict of interest waivers have been issued in connection with this meeting. To ensure transparency, we encourage all committee members to disclose any public statements that they have made concerning the issues before the committee.

With respect to FDA's invited industry

representatives, we would like to disclose that Drs. Daniel Heck and John Lauterbach and Mr. Arnold Hamm are participating in this meeting as non-voting industry representatives acting on behalf of the interests of the tobacco manufacturing industry and the small business tobacco manufacturing industry and tobacco growers respectively. Their role at this meeting is to represent these industries in general and not any particular company. Dr. Heck is employed by Lorillard Tobacco Company, Dr. Lauterbach is employed by Lauterbach & Associates, LLC, and Mr. Hamm is retired.

I'd like to ask you to please silence your cell phones if you have not already done so, and I'd like to introduce our press contacts, Tesfa Alexander and Jeffrey Ventura. If you're here, please stand up. Thank you.

Introduction of Committee Members

DR. SAMET: Great. Okay. Thank you. Good morning. And let me now ask the committee to introduce themselves. Let's start I think with the phone.

Melanie, you're still with us?

DR. WAKEFIELD: Yes, Melanie Wakefield, Cancer Council Victoria in Melbourne, Australia.

DR. SAMET: All right. Neal?

DR. BENOWITZ: Neal Benowitz, University of California, San Francisco.

DR. SAMET: Okay. Karen, we'll start left.

MS. DELEEUW: Karen DeLeeuw, Colorado Department of Public Health and Environment.

DR. HENNINGFIELD: Jack Henningfield, Pinney Associates and Johns Hopkins University School of Medicine.

DR. NEZ HENDERSON: Patricia Nez Henderson, Black Hills Center for American Indian Health.

DR. CLANTON: Mark Clanton, representing pediatrics, public health and oncology.

DR. HATSUKAMI: Dorothy Hatsukami from the University of Minnesota.

DR. MCAFEE: Tim McAfee from the Center for Disease Control.

DR. HECK: Dan Heck from Lorillard Tobacco Company, representing the manufacturers.

DR. LAUTERBACH: John Lauterbach, Lauterbach & Associates, representing small business tobacco manufacturers.

MR. HAMM: Arnold Hamm, representing U.S. tobacco growers.

DR. SAMET: Okay. Thank you. Actually, when Caryn read the statement, I thought it sounded like Dan had moved to work for Lauterbach & Associates.

DR. LAUTERBACH: Anytime.

DR. SAMET: Okay. Corinne, I think you're going to move next.

DR. HUSTEN: Corinne Husten, Center for Tobacco Products.

DR. ASHLEY: David Ashley, Center for Tobacco Products.

DR. DEYTON: And Lawrence Deyton, Center for Tobacco Products.

FDA Presentation: The Menthol Report

DR. HUSTEN: The subcommittee and working groups have completed their drafting of the TPSAC report on the public health impact of menthol

cigarettes. The chapters of the report are being posted to the FDA website; a redacted hard copy of the chapters will be available shortly in a binder at the table just outside the meeting room. We've made copies of the chapters available for the participants at the table. Unredacted copies of the draft report were distributed electronically to the TPSAC voting members early this morning for their review. Redacted versions were sent to the industry representatives as soon as the redaction was completed.

It's our understanding that TPSAC plans to come to closure on the report on the conclusion of this morning's meeting after deliberating on a draft report and the recommendations. If there are substantive changes to the scientific evidence or chapter conclusions proposed by the committee to the report that cannot be incorporated into the document during today's meeting, FDA will be happy to organize an additional brief public session of the TPSAC before March 23rd for the committee to review and discuss the changes made to the report.

If after its deliberation, the TPSAC adopts the draft report, it will be considered submitted to FDA. After submission, no substantive changes in scientific findings, conclusions or recommendations will be made to the report. Clerical support has been provided to the committee for assistance in proofreading and formatting of the document, including incorporating verbatim the TPSAC recommendations into the final report. The submitted TPSAC report will be reviewed again by FDA staff to ensure that decisions about current redaction of trade secret and commercial confidential information are correct. At that time, the final report of the full committee will be posted on the FDA website.

DR. SAMET: Thank you.

So our task this morning is to complete our discussion of the chapters of the report, including of course chapter 8, which provides our answers to the seven questions listed here as well as the two additional questions at the population level, our overall findings and recommendations as well as

discussion of some additional issues.

I think what we'll do is return first to discussion of chapter 6, which has now been brought to completion. And, Dorothy, I'll turn to you to take the lead.

DR. HATUSKMI: So basically, as I mentioned before yesterday, there are three areas that we examined. One was initiation and experimentation. And within that area, we were asked to answer the question is there evidence to indicate that the availability of menthol cigarettes increases the likelihood of experimentation and initiation.

To take a look at that issue, what we wanted to do is take a look at the proportion of menthol users across the age spectrum. And what we had observed was that there were considerably a higher number of younger population of smokers compared to the older population of smokers that smoke menthol cigarettes among smokers. The only exception was African Americans for whom the rates were high during adolescence as well as during the older age.

We also looked at the portion of adolescent

smokers who smoked menthol cigarettes among the population of youth smokers. And even within that particular population, we found evidence that was sufficient to conclude that the rate of menthol users are highest among the younger users and then decreases over age.

The second evidence that we looked at was the trend of menthol use among the adolescent population, and what we observed is that there is an increasing trend of menthol cigarette smoking among the youth. And this coincides with the decreasing trend of non-menthol cigarette use among the adolescent smokers. And so we were particularly concerned about this trend.

We addressed the issue of the fact that cigarette smoking is becoming less prevalent among the adolescents. This was raised by some of the members of the tobacco company, but we believed that there is sufficient evidence to conclude that menthol cigarettes is declining at a slower rate than non-menthol cigarette smoking.

We looked at the proportion of adolescent

smokers who smoke menthol among the less established smokers, and that was defined as smoking for less than one year and compared it to more established smokers; that is, smoking for greater than one year. And we found that there were a higher number of adolescent smokers who smoked menthol cigarettes among those who were less established smokers compared to more established smokers, meaning that the less experienced adolescent smokers may, in fact, be experimenting with menthol cigarettes.

We looked at the age of initiation of menthol versus non-menthol cigarettes, and we found that there were no differences in terms of the age of initiation. However, we did find one study that was conducted by Curtin et al. from RJR that showed that adolescents tended to smoke at an earlier age.

We also found evidence based on concordant findings from studies of internal tobacco industry documents. So these were studies that were conducted by independent investigators that the tobacco companies were aware of the appeal of

menthol cigarettes to younger novice smokers because these cigarettes were indeed easier to smoke, which coincides with the biological plausibility that was found in chapter 3.

So the other area that we addressed was addiction, and the first question that we addressed was does the availability of menthol cigarettes increase the likelihood of becoming addicted? And to date, there's been one unpublished secondary analysis that has addressed this issue in a sample of adolescent students who were assessed from different regions of the country, the U.S. And this study strongly suggests that menthol cigarettes are associated with increased transition to greater or established smoking and dependence.

The second issue that we addressed in the addiction was does the inclusion of menthol in cigarettes increase the degree of addiction in smokers compared to non-smokers. So we looked at a number of areas to address this issue. Among the adult studies, we looked at the pharmacokinetics of nicotine.

We've looked at abuse liability studies, cigarette smoked per day, exposure to nicotine in general, exposure to nicotine per cigarette, as well as subjective measures of dependence. And like Dr. Heck's report, we found that among adults, there isn't any evidence to support that adults are more addicted to menthol cigarettes compared to those who smoke non-menthol cigarettes. However, we did take a look at a body of literature related to adolescents, and we felt that there was enough evidence to conclude that among the adolescent population, that they tend to experience not only a higher prevalence of addiction but also more severe addiction than among non-menthol smokers. And this is of concern because this is a population that's particularly vulnerable to the effects of menthol cigarette smoking.

With regards to the area of cessation, we did take a look at all the scientific literature, and you could probably tell by the thickness of the report. And so we just wanted to make sure that the FDA had all the information available to them

to see how we came to our conclusion. And in the evaluation of this cessation studies, we more heavily weighted the population surveys. And the reason why we did is because the majority of people that quit smoking, quit smoking on their own. They don't necessarily enter treatment to quit smoking. So that's where we put most of the emphasis in terms of the extent to which we used the evidence to make our determination.

Based upon that particular criteria as well as other criteria that you will see specified in the report, we think that there is sufficient evidence to show that non-white smokers actually who smoke menthol cigarettes experience more difficulty quitting than non-white smokers that smoke non-menthol cigarettes.

The information on the whites is mixed, and unlike the tobacco industry report, we felt that it was really important to concentrate on looking at studies that examined the different racial ethnic groups primarily because certain racial ethnic groups may in fact have different experiences with

menthol cigarettes. And, in part, it was our charge given – a charge given to TPSAC to take a look at racial ethnic differences.

Now, there were some studies to suggest, as I had noted in our previous meeting, that the menthol cigarette smokers tend to be less responsive to medication. And this we believe is an area for further exploration. Unfortunately, there were no studies that have been conducted with adolescent smokers to compare the differences between menthol and non-menthol cigarettes on smoking cessation.

Finally, we believe that menthol cigarettes are marketed toward the African-American population and the young, and this was pointed out by chapter 5. And this was a real concern to us because these are often the groups that are at high risk for poor cessation outcomes. So that was our report.

DR. SAMET: Okay. Thank you.

Of course, this is a very lengthy chapter. Just for those of you who may not have it, there are 49 pages of text as well as extensive

supporting tables. So let me open for discussion, question, comments.

Dan.

DR. HECK: Just a slight clarification to the summary. I thought I heard correctly reference to the industry menthol report not addressing the cessation studies for specific ethnic subpopulations. That discussion is in the report. I'm sorry if it didn't make it or wasn't clear in the executive summary, so we'll have that next week.

DR. SAMET: Okay. Thank you. And, of course, we'll look forward to reading the full report.

Let me see. Other questions -- Neal or Melanie?

DR. WAKEFIELD: I don't have any questions, Jon.

DR. BENOWITZ: I don't, either, Jon.

DR. SAMET: Okay. Does, again, anyone else around the table have further questions or comments on this chapter?

[No response.]

DR. SAMET: Dorothy?

DR. HATSUKAMI: I do want to mention an erratum. Dr. Heck had yesterday -- when we were discussing the Nonnemaker article, he had said that 1.68 was not significant, and you're right. And we did take a look at the population that did not include wave 3. And I realize the reason why we did that is because we wanted to be more conservative in our estimate. If we chose the significant value, then the odds ratio would have been much higher. And so we were more conservative in terms of the estimate. So I apologize for misleading the committee as well as Dr. Heck.

DR. HECK: Yes, as a follow-on to that, I'd have to look carefully at the calculations because I'm recalling the calculation comes out to over 100 percent initiation if all the data are included. So it just seemed to be contrary to common sense, and we'll have to look carefully at the model, though, I think.

DR. SAMET: Yes, an actual comment, I think

this is where the sensitivity analyses that are provided in the appendix are important so that you can gauge the consequences of any particular assumption. Of course, there is an estimate of 1.00 for that particular parameter included for comparison.

Okay. Then I think we're done with chapter 6. We'll turn to chapter 8, which is the conclusions and recommendations chapter. And Mark will lead that discussion.

Presentation and Discussion of

Final Menthol Report and Recommendations

DR. CLANTON: Thank you.

The plan to discuss chapter 8 is as follows. I'm going to provide an introduction to the chapteri. We're going to review the questions that were posed on both the population and individual level. I'll provide the finding for each of these questions, and then we'll summarize with future research recommendations and a recommendation to the FDA.

By way of introduction, in this chapter,

TPSAC synthesized the evidence included in chapters 3 to 6 to address the charge given to TPSAC in the Act. Using the methodology described in chapter 2, TPSAC has systematically identified and evaluated relevant studies and other evidence, including papers published in the peer-reviewed literature, documents supplied to the committee by tobacco companies, FDA white papers, and unpublished tobacco company documents.

Here, TPSAC provides its conclusions to the seven key questions in chapter 1 related to individual smokers and the two key questions related to effects at the population level. These conclusions are expressed in the classification set out in chapter 2 that is based around the anchoring point of equipoise in the strength of evidence for and against a relationship.

The answer to these questions underlies TPSAC's qualitative judgment as to whether there is an adverse impact on public health from menthol cigarettes. The results of models are used to provide a quantitative picture of the adverse

impact. Because the answers to questions 1 and 2 utilize the same evidence, these closely-related questions are answered together. For the same reason, questions 3 and 4, which are also closely related, are answered together. Chapter 8 concludes with recommendations to the FDA and a discussion of contraband as called for under Section 907(b).

Evidence synthesis for key questions. Questions related to individual smokers. Number 1, does the availability of menthol cigarettes increase the likelihood of experimentation? And question 2, does the availability of menthol cigarettes increase the likelihood of becoming a regular smoker?

TPSAC finds based its review that the evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes increases experimentation and regular smoking. In the jargon and lexicon of equipoise, it is considered above the equipoise level.

Question 3. Does inclusion of menthol in

cigarettes increase the likelihood of smokers becoming addicted? Question 4. Does inclusion of menthol in cigarettes increase the degree of addiction of the smoker?

Here, TPSAC finds, first, the evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes increases the likelihood of addiction and the degree of addiction in youth smokers above equipoise. And there is insufficient evidence to conclude that menthol cigarettes increased the likelihood of addiction and the severity of addiction in adults. The evidence was below equipoise.

Adding additional information for 3 and 4 and the rationale for the conclusion, TPSAC found clear evidence of a relationship between menthol cigarettes and nicotine addiction in youth. This evidence presented in chapters 3 and 6 provide three key findings. I will mention two of them.

Youth who initiate with menthol cigarettes are more likely to become daily regular or

established smokers than youth who initiate with non-menthol cigarettes. And second, adolescent menthol cigarette smokers have a higher prevalence of nicotine dependence and degree of addiction than in those who smoke non-menthol cigarettes.

Question number 5. Are smokers of menthol cigarettes less likely to quit successfully than smokers of non-menthol cigarettes? Here, TPSAC has the following finding.

The evidence is sufficient to conclude that a relationship is more likely than not that the availability of menthol cigarettes results in lower likelihood of smoking cessation in African Americans compared to non-menthol cigarettes. The evidence was judged to be above equipoise. And 2, the evidence is sufficient to conclude that a relationship is as likely as not that the availability of menthol cigarettes results in lower likelihood of smoking cessation success in other racial and ethnic groups. The evidence was judged to be at the equipoise level, as likely as not.

An additional comment here, TPSAC examined

data from national population surveys and other studies to determine the comparative success of quit attempts among smokers of menthol compared with non-menthol cigarettes. This information is summarized in chapter 6.

Number 6. Do biomarker studies indicate that smokers of menthol cigarettes receive greater doses of harmful agents per cigarette smoked compared with smokers of non-menthol cigarettes? Here, TPSAC finds the evidence is insufficient to conclude that it is more likely than not that menthol smokers inhale more smoke per cigarette or that they're exposed to higher levels of nicotine or other tobacco toxins. The evidence was judged below equipoise.

Number 7. Do smokers of menthol cigarettes have increased risk for diseases caused by smoking compared to smokers of non-menthol cigarettes? Once again, TPSAC finds the evidence is insufficient to conclude that it is more likely than not that smokers of menthol cigarettes have increased risk for disease caused by smoking

menthol cigarettes compared to non-menthol cigarette smokers. The evidence was judged to be below equipoise.

Now on to the two questions that refer to the population level. Number 1. Does the availability of menthol cigarettes increase the prevalence of smoking in the population beyond the anticipated prevalence if such cigarettes were not available? The question also asked a similar question in subgroups within the population.

Here, TPSAC finds that the evidence is sufficient to conclude that it is more likely than not that the availability of menthol cigarettes increases the likelihood of experimentation and regular smoking beyond the anticipated prevalence if such cigarettes were not available in the general population and, in particular, available to African Americans.

The evidence is sufficient to conclude that is more likely than not there is a causal relationship between the availability of menthol cigarettes and regular smoking among youth. The

evidence was judged to be above equipoise.

Moving now to the second question for the population level, does tobacco company marketing of menthol cigarettes increase the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available? Also, applied in the subgroup population.

Here, TPSAC found the following three points. The evidence is sufficient to conclude that it is more likely than not that menthol cigarette marketing increases the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available for the whole population for youth and for African Americans. The evidence was judged here to be above equipoise.

Number 2. The evidence is sufficient to conclude that it is as likely as not that menthol cigarettes increase prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available. The evidence was judged to be at equipoise, as likely as not. And lastly, TPSAC finds the evidence is insufficient to conclude that

it is more likely than not that menthol cigarette marketing increases the prevalence of smoking beyond the anticipated prevalence if such cigarettes were not available for Asian Americans, Hawaiian Pacific Islanders and women. The evidence was judged to be below equipoise.

And now for the overall conclusions. There were two. First, menthol cigarettes have an adverse impact on the public health in the United States. Number 2, there are no public health benefits of menthol compared to non-menthol cigarettes.

There's a section that then summarizes the model as it provides wisdom as it relates to the potential quantitative public health impact of menthol cigarettes versus non-menthol cigarettes. That is summarized, and I'm going to read this portion of the recommendation.

"Mentholation of cigarettes was discovered by accident in 1920. Even then, the sensory and medicinal properties of menthol were known, and these properties along with cigarette design and

marketing have made menthol cigarettes a substantial component of the cigarette market in the United States. In the decades since the first menthol cigarettes were made, there have been substantial advances in the understanding of the pharmacology of menthol, of how to use menthol to manipulate flavor and the sensory perception of cigarette smoke and of the interplay between menthol and nicotine.

TPSAC has found that the availability of menthol cigarettes has an adverse impact on the public health by increasing the number of smokers with the resulting premature death and avoidable mortality."

We make the following overall recommendations. Actually, first, I'm going to just make a couple of comments about contraband. As you recall, Section 907(b) requires that the Secretary pay close attention and make provisions for issues related to contraband.

Our conclusions here are the following: After reviewing several presentations on contraband

and counterfeiting, TPSAC acknowledges that the potential for contraband menthol cigarettes exist. Should FDA choose to implement a ban or take some other policy action that restricts the availability of menthol cigarettes, consistent with the requirements of the Act, TPSAC recommends that the FDA consult with the appropriate experts and carry out relevant analyses depending on the actions taken in response to this report from TPSAC. At present, TPSAC is not constituted to carry out such analyses, and lacking knowledge of FDA's intent on the receipt of this report, it concluded that the FDA would need to assess the potential for contraband menthol cigarettes as required by the Act.

We have a section on other considerations, which you can read, and I would like to conclude with recommendations on future research. In the course of reviewing the evidence related to its charge, TPSAC noted gaps in the understanding of menthol cigarettes and public health that should be addressed with future research. Here, TPSAC makes

brief recommendations with acknowledgement that the priority given to particular recommendations may depend on any policy action taken by the FDA.

First, on the topic of subliminal menthol, TPSAC was given the charge of addressing menthol in cigarettes but, as set out in chapter 1, focused this report on menthol cigarettes. Several studies suggest that menthol may be present in some cigarettes in which it is not a characterizing additive.

TPSAC suggests that future and further research should be carried out to characterize the menthol content of cigarettes in general and to assess whether menthol has pharmacologic effects at these concentrations that might affect initiation, dependence and cessation.

Next, under the topic of susceptible and vulnerable populations, TPSAC found little data on the use of menthol cigarettes by severely ill -- a population with a high prevalence of cigarette smoking. This gap should be addressed as should data gaps for other potentially vulnerable

populations. There is now substantial research on genetic determinants of addiction to nicotine. Studies on this topic should incorporate consideration of menthol cigarette smoking in their protocol.

In addition, more research is required to assess whether menthol interacts with genetically determined bitterness taste sensitivity such as the taste sensitivity to PTC, which is phenylthiocarbamate, or PROP, which is 6-n-propylthiouracil, to facilitate smoking.

Lastly, under the category of strengthen the evidence foundation on the public health impact of menthol cigarettes, first, cohort studies of adolescents and youth adults should be carried that follow participants from experimentation to initiation to dependence. These studies would provide an important understanding of the risk for moving across this sequence that is associated with menthol cigarette availability.

Number 2. The consequences of menthol cigarette smoking for likelihood of successful

cessation need further investigation in the general population. Additionally, the implications of menthol cigarettes for sustained quitting should be addressed in clinical trials of cessation therapy as well as other databases.

And lastly, we recommend that there should be developed surveillance protocols to track industry marketing practices, including price promotions and their impact on smoking patterns with attention to menthol cigarettes. The protocols should be sufficiently fine-grained with regard to populations and places and focuses on critical periods of policy implementation.

We'll go back to one point. Consequently, TPSAC makes the following overall recommendation to the FDA. Removal of menthol cigarettes from the marketplace would benefit public health in the United States. The Act offers a variety of mechanism for the FDA to consider. If it concludes that it should pursue this recommendation at this time, TPSAC has no specific suggestions for follow-up by FDA to the recommendation.

Committee Discussion of

Questions to the Committee

DR. SAMET: Okay. Thank you, Mark.

Now this is open for discussion, and I'd particularly like to hear from the member who was not in the writing group. Jack.

DR. HENNINGFIELD: Just to go to a smaller point rather than starting with the big one, before this committee started, it had been well accepted that menthol smoking initiation led to menthol smoking in adults. I think one of the findings that was troubling for me was seeing the data be laid out that menthol smoking initiation also led to increases in the general population beyond menthol smokers, in other words, that there were people that started on menthol, then switched to non-menthol. And that means that menthol is contributing to overall population prevalence on top of menthol smokers and disease in people who are not menthol users.

Some people -- and there has been discussion of this -- would characterize menthol cigarettes

then as a starter product in that sense. The word "starter product" wasn't used in this report. I suspect some readers will use that term. What's your own sense? Is that a term that you think is appropriate or just a general term that's not scientific enough or?

DR. CLANTON: Well, let me try to respond to both questions. So first of all, if you just look at basic switching rates, the switching rate from menthol to non-menthol is fairly low, in the range of 5, 6 percent. However, we did find evidence that those who initiate with menthol, that there may be as much as a 28 percent switch to a non-menthol cigarette at some point after they become a regular smoker. A lot of the switching has to do with when you're measuring it and what that looks like. So typically it looks low, but we did have evidence that as much as almost a third of those who might initiate with a menthol cigarette at some point in their adult regular smoking would then go on to non-menthol cigarettes.

So your point is well taken that at least at

a third level, we find that there are people who are starting with menthol and then moving on. We can probably have further discussion about whether or not it should be called a starter cigarette.

Should it be a third, should we see 50 percent level transitioning to non-menthol, should it be 75 percent transition, I don't know the answer. But I can give you quantitatively, it's about a third, and whether or not it would be called a starter cigarette is open for discussion.

DR. SAMET: I'm going to say, Jack, partly in response to your comment, it was certainly not a term that we either considered nor used as the evidence was being reviewed. I mean, I think the evidence review was really strictly focused on the questions. So I think any additional sort of surmise would lie with those who want to take the evidence further.

Dorothy, did you want to comment?

DR. HATSUKAMI: We do talk about the rate of switching in chapter 6. I just didn't bring it up in my summary, but Mark has done a good

recapitulation of that information.

DR. SAMET: Jack, further comments on the report?

DR. HENNINGFIELD: On the general contraband issue, I think that the report appropriately points out the limitations of the committee. The report certainly has listened -- I think it's evident that the committee has listened and the report addresses those concerns. And any feeling that they've been ignored I think is not consistent with the report.

I think that the recommendations to FDA as to things to consider are succinct and appropriate. I think that FDA might also be looking at countries and regions in which menthol cigarettes are not marketed. I'm not sure if they're actually banned in any of those, but to see -- I'm not aware that there is a contraband problem in those areas. And it's something that FDA should look at, because if there isn't a contraband problem that is major in regions where it's not marketed or not banned, FDA might learn from what is happening.

Related to that, we know that marketing is

important, and so one of the limitations of any model is a world without or a country without marketing. So my guess is that the models underestimate the potential benefits because marketing would also not be allowed. So that's something to be looked at.

Lastly is the benefits of the education. And so, for example, when you look at the findings that have just been discussed and conclusions, if conclusions such as those were part of an education program before any action was taken, if an action was taken and after, those effects would be expected on the basis of everything we know about smoking and other drug use to reduce demand. And so I think FDA when looking at the contraband issue is going to have to think about not only how do you reduce the supply but how do you reduce demand. And I think what's unraveling globally with the international treaty provides some lessons there as well.

DR. SAMET: I think you captured the general approach to the contraband issue well. I think we

recognized that this was in our charge. We were certainly reminded of that by public commenters. We were provided with a number of potential scenarios of what might follow, based on necessarily a lack of knowledge of what steps FDA might take in the future with regard to menthol cigarettes. And I think that's why we feel that our job at this point is to call attention of the FDA to this issue, express the concern, acknowledge the possibility, and then leave open. Depending, as you point out, whatever the future actions may be, the issue would need to receive attention under the circumstances of those actions.

Dan.

DR. HECK: I did notice, in just the few minutes I've had to absorb the concluding chapter here, some points of agreement between the industry menthol report and the voting members' report. I note that these areas of agreement, broad agreement, tend to come from the areas of the traditional quantifiable hard sciences and extending that also to the risk. There doesn't --

I think there's broad agreement that menthol cigarettes don't seem to convey greater individual risk to the smoker, and the population risk from epi studies seem to concur with that.

I think another point of agreement here in the research recommendations, they call for strengthening of evidence in the area of the transition of smoking experimentation to initiators of a long-term smoking habit. Particularly, as I tried to express yesterday, the model presented by the committee, whether that key figure appears to be derived from a single study, the Nonnemaker study, yet unpublished and un-peer reviewed, of a relatively small adolescent population, just over 100 I believe with, again, around a dozen African Americans. So I think we do have an acute need to improve the quality of our knowledge and science of that particular step or stage of the smoking initiation process.

I think what your points of disagreement that we have are certainly on these behavioral areas, some of the initiation, dependence,

cessation areas where we're asked to, in effect, try to infer causation by menthol of these very complex human behaviors. And in the industry's view, as I expressed yesterday, and as you'll see in our report, we don't feel that the science in those areas is sufficient to support a sound regulatory science judgment. They may be unknowable in terms of a single factor such as preference for menthol in terms of a causal role.

So I think that's a point of disagreement between the two reports, but FDA will have the opportunity to consider both and consider the additional evidence that's coming into the literature going forward.

DR. SAMET: Thank you, Dan. I think all of us here have taken a close look at the large literature and recognize its complexities. And I think certainly TPSAC has worked very hard to try and understand the main findings and the level of evidence across this body of literature, as you and your colleagues have. And you are correct; these reports and whatever other reports may be submitted

to FDA will be considered by them.

Let me see. We have Melanie and Neal on the phone, and if either of you are awake and want to comment, now would be a good time.

DR. WAKEFIELD: It's Melanie. I'm fine. Thanks, Jon, and I'm still awake.

DR. SAMET: Okay. Great, and it's been a long time for you. We recognize.

Neal?

DR. BENOWITZ: No comments, Jon.

DR. SAMET: Okay. Thank you.

Let me ask if there are any other comments then before we come close to ending this session. I think I have a few remarks in closing, and then I guess we'll move to Bopper. So anything else? Tim? Yes?

DR. MCAFEE: First, I want to express the appreciation for somebody who is an ex officio government representative on the committee but did not have to take part in the actual work of producing the report. I want to thank the -- although part of our job in terms of the CDC and

the other government members is that we all have to work over the ensuing years to actually deal with the recommendations of the committee, so you might not like my job a year from now.

But anyway, thank you very much for all the effort and thought you did on this very difficult and challenging area. And I just wanted to make one or two brief remarks about this and essentially redraw our attention to a point that I've made a couple times around this, which I think one of the things that was challenging about your job, that was essentially imposed because the interpretation of the regulatory framework, was the need to create a counterfactual model that essentially was predicated on the idea that menthol didn't exist or hadn't existed.

Therefore because of that, the modeling of what the world would look like that Dr. Mendez painstakingly put forward is in fact a conservative -- even given the use of the conservative assumptions, from a public health perspective, which is the other element that

Congress tasked FDA with, this is an extremely conservative estimate of the public health benefit of an actual taking menthol out of cigarettes because, in fact, if we look at the -- for instance, the model that David Levy used, which actually tried to estimate what would actually happen during a transition period relating to the role of menthol, the effects are much larger.

So even with the conservative model, which ends up with 40 to 60,000 deaths averted in African Americans and hundreds of thousands in the general population, these are clearly -- and actually I think, to the tobacco industry's credit, they actually acknowledged this in their executive summary and several of the statements that were made, which is removal of menthol cigarettes from the market plausibly would have some public health benefit. Removing any type of cigarette preferred by a substantial number of Americans might result in some smokers quitting when their preferred type of cigarette is taken away by the government.

So again, this may not be the primary

rationale from a regulatory perspective for why it would make sense or not make sense to take menthol out, but just as the industry is insisting that the FDA consider the essentially unanticipated side effects of the creation of a contraband market, I would encourage the FDA to, in its deliberations about what to do with this report, also take into consideration essentially the public health side effects that this move would have in the U.S. population and particularly for African Americans and youth, where the effect sizes will almost certainly be substantially larger than those that the committee used to make its decision.

Again, finally, I would just again echo the point, I think the committee, given its expertise, did the best job that it could over the issue of contraband and that this is something that clearly should be addressed in the FDA's consideration. I think it will be difficult to do, and most of the modeling that we heard about was based on price, data derived on price. And I think that it is not clear that that will be directly correlated with

menthol and that there are many other things that would be specific around this.

Be that as it may, the other issue is that this is again an area where I think in fact some of the interests of the tobacco industry and public health and FDA could potentially be aligned if this moves forward because, as has been noted, it is not in the interest of public health, governmental entities, et cetera, to see a large increase in contraband. But that is not a static mechanism, that there are many steps that government could take and the tobacco industry could take to markedly diminish what is really still a modest problem in our country, that the vast majority of cigarettes are still being purchased through legal mechanisms.

The only other thing that I think grated in this that is important to point out is it is a fundamental error to talk about legal versus illegal sales to minors. All sales to minors are contraband, period. So that should be off the table.

So I think looking at things that can be done around packaging at the manufacturing level that will make it easier for agents at the state and federal level to track this is well worth our attention, and it does not have to be an area where there is significant contention.

So again, thank you very much for your efforts over the past 10 meetings.

DR. SAMET: Thank you, Tim.

Patricia.

DR. NEZ HENDERSON: At the beginning of this meeting back in March of 2010, I used a phrase that on the Navajo nation we use when we talked about commercial tobacco, (speaking native language), meaning however you use commercial tobacco, it is harmful for you and everybody around you. And I'm very grateful today that this recommendation has been put together by our team, and that's all I wanted to say on behalf of the public.

DR. SAMET: Thank you, Patricia.

Dan.

DR. HECK: Just one quick follow-up. I

thank Dr. McAfee for reminding me of the point that is discussed in somewhat greater length in the industry report, and that is we're aware. We know that menthol cigarettes are preferred by a significant minority of smokers, about 30 percent overall, and predominantly preferred among the African-American community.

We don't need a model to project that the elimination of any segment of the tobacco product market would be projected to displease persons who favor those cigarettes, and I think light cigarettes are the biggest example by far, the most popular segment now.

But the industry's perspective there is that this is not the question we're about. The law, as I understand it as a non-lawyer, constrains the new regulatory authority from banning cigarettes, eliminating cigarettes totally, although the scientific basis for regulation does indeed empower FDA to regulate the content, emissions, product design elements and such.

So again, I don't think we need a model to

project the reality represented in the summary here, that any segment of the market, potentially eliminated or the what-if scenarios had it never existed or did not exist in the future, could probably be interpreted as having an affirmative public health benefit.

Just one point on that with regard to youth smoking or adult smoking for that matter, I want to remind FDA when we present this information to them, as has been presented before, we have examples around the world of many markets where menthol cigarettes effectively do not exist, a market share well below at 1 percent as it can be measured by the surveys in those countries.

We do not see low youth smoking or adult smoking. In fact, we see markedly higher youth smoking in many of those countries. We see that same pattern across the U.S. states as we've presented. The menthol market presence is inversely related in a modest but statistically significant way to youth smoking. So I think we should temper our expectations of the effect of one

regulatory scenario or another with the realities that are presented to us by real-world information, both internationally and from the states.

DR. SAMET: Thank you.

Any other comments? Tim?

DR. MCAFEE: I would fully concur with Dr. Heck's point that we do not think that eliminating menthol -- or if menthol were eliminated that that would be the end of the public health problems associated with tobacco use. But we are at a unique situation in the United States because of the prevalence of menthol is so high. And I think this is a very important point that Dr. Hatsukami laid out, that essentially the -- and this was interesting to me quickly reading your report because I saw it at the same time you did, that in fact the concern is in the trend, that although adolescent use and adult prevalence is declining, that the rate of decline is slower among menthol. So there appears to be something going on there.

DR. SAMET: Thank you.

Jack.

DR. HENNINGFIELD: Just very briefly on the international experience, which I think we learned from the international experience, and in turn other nations will learn from what is happening here, we know that overall rates of tobacco use and initiation are related to comprehensive tobacco control costs, social attitudes, history and so forth. So comparing the cross-nations in that sense, I don't think is necessarily useful. I think the important thing, though, is that there are many nations and regions where menthol use is extremely low, as you acknowledged, 1 percent or less, and there is not a huge contraband problem. And I think that's where it is important for FDA going forward to see why that is so low. Maybe the situation here would be a much lower contraband problem than has been predicted by some.

DR. SAMET: Thank you, Jack.

Let me just make sure that we have no more questions or comments. So I assume Neal and Melanie, nothing more from you?

DR. WAKEFIELD: I'm good. Thanks.

DR. BENOWITZ: Not from me.

DR. SAMET: Okay. And no one else. Well, very good.

So I actually have a few last concluding remarks. I think probably this moment in a year-long journey deserves at least a few closing comments. First, the report does have a name beyond the menthol report, and the title is Menthol Cigarettes and the Public Health: Review of the Scientific Evidence and Recommendations, a rather straightforward description of what the report is about.

I just wanted to remind everyone -- and I think the committee certainly is aware -- that this report reflects work done over 10 meetings that began almost a year ago. To use the cliché, it's been a long journey, and at least for TPSAC on this particular report, we will be done with any final editorial cleanup by March 23rd.

Just a few comments about the process over this year, I think for those of you who have

watched it, it has had many unique characteristics. It's been transparent. It's been open. We've posted our drafts and entered into a dialogue with many stakeholders on this important issue. We've had very helpful input from a variety of commenters, and on our request, materials have been made available from the tobacco industry.

TPSAC includes non-voting representatives from the tobacco industry, three colleagues, Arnold, John and Dan, and I think we've had a collegial and helpful dialogue with you, and we appreciate your input. And clearly you have very valuable and deep knowledge on this topic.

I think just some broad thanks. We've had many people who have brought comments to us from a variety of sectors ranging from the industry to various stakeholder groups and the public health community. A vast amount of scholarship has been done, I think much of it carried to support our activities; for example, the reviews of the tobacco industry documents, special issues to journals on the topic of menthol and so on. And these were

certainly valuable for us as we pursued our tasks.

So I want to thank all of those who have brought information to us and I think at the broader run of commenters who have made clear the societal importance of this issue and its importance to particular groups within the population.

FDA staff, I think you have to remember that about the time we got started on our report, FDA did not particularly have very many staff. And over the year since then, the FDA team has grown and I think always been extremely helpful to our efforts, and we thank all of you for your support. I don't think we've been too demanding a committee, actually, but you may see it differently. That will be an offline discussion.

We've had support from Denise Gellene, who helped us edit this document. This has been written quickly and taken support, needed editorial support, to bring it into shape. And that refinement will continue up to the last moment to deal with I think what are inevitable editorial

problems when a large document is produced relatively quickly.

David Mendez, we appreciate your work and effort in extending your prior work on tobacco modeling to include menthol. I think that work has provided a useful gauge as to the public health impact of menthol cigarettes.

I think last, to the committee, the writing committee. Jack, I don't know how you escaped not being on the writing committee, but I guess somebody had to have that job. But we appreciate of course your comments.

I think for those of us who have worked together on this report, it's been somewhat of a bonding experience, if you will. And there's been a lot of work in exchange and communication among us. So I appreciate all of your efforts. I think I know everyone has dug deep to get this done, and I think hopefully it shows in the quality of the report that we've produced.

We've had to digest and reach conclusions based on a very diverse body of evidence, a very

complicated set of scientific literature. And we needed to interweave these lines of science to reach the conclusions that there were, and I think that interweaving has taken a lot of thoughtful work on your parts, and I appreciate those efforts. So thanks to you all on the writing subcommittee.

So with that said, we've completed our tasks, and I think at this point the FDA has our findings and recommendations and suggestions. And we'll watch with interest what next steps you will take, as of course will many others. So let me turn things to Bopper.

DR. DEYTON: Mr. Chairman and really to the whole committee, as you know, I've attended all of your meetings, and it has been a very impressive process to watch, how this committee has handled a very difficult and complex task. And I think we all appreciate the amazing amount of work that has gone on.

By discussing and finalizing your report and recommendations, the committee is now near completion of your first charge under the Tobacco

Control Act, evaluating the available scientific evidence on the impact of the use of menthol in cigarettes and the impact on public health. So by completing your charge, it doesn't mark the end of a process. It does mean we've reached a very important milestone, though, today.

The Tobacco Control Act requires you to submit this report to FDA by March 23rd, and it looks like you will make that deadline. It has been a long year, and it's nice to be at that milestone. But I need to be very clear that the TPSAC final report is advice to FDA. The report does not set FDA policy. It does not set FDA actions, and FDA's receipt of the final report will not have a direct and immediate effect on the availability of menthol products.

Once the final report is received by FDA, obviously it will undergo thorough expert review by our staff. But FDA work will be to assess all of the science related to these issues as applied to the standards outlined in the Tobacco Control Act. Those include the population impact of menthol in

cigarettes; the risks and benefits to the population as a whole, users and nonusers alike. We'll examine effects on overall smoking initiation and cessation rates. And if considering any new product standards, we will assess the technical achievability and possible countervailing effects, such as creation of demand for contraband and the other issues that we've discussed here.

Now, although there is no required deadline or timeline for FDA to act on the issue of menthol in cigarettes, we do recognize the strong interest in this issue and will continue to communicate the steps FDA is taking as we undertake our work now as we determine what, if any, future regulatory actions are warranted.

We intend to provide our first progress report on our review of the science in approximately 90 days. Ultimately, FDA's decision whether to implement any of the report's recommendations will be driven first and foremost by our commitment to reduce the toll of disease, disability and death caused by tobacco in the U.S.

and the requirements of the Tobacco Control Act.

So on behalf of Commissioner Hamburg and all of us here at the Center for Tobacco Products, I want to thank each member of TPSAC for all the time, the expertise, and the effort that you have put into this important process over the last year. I also want to thank members of the public who've attended these meetings and who have offered their very helpful comments. But now it's up to us to do our job, and I want to thank you for doing yours.

Adjournment

DR. SAMET: Thank you, Bopper, and we will obviously watch with interest. I think we don't have a TPSAC meeting until July, and so we will have a -- I think this is a TPSAC vacation almost, and we look forward to it.

So again, thank you, and as Bopper pointed out, we've done our first task. I guess others await us, as we know. So meeting adjourned.

(Whereupon, at 9:21 a.m., the meeting was adjourned.)